CLAIMS

We claim:

1. A method for screening for a bioactive agent capable of modulating USP-25 protein activity, comprising:

a) combining a USP-25 protein, a USP-25 target protein which is conjugated to ubiquitin or ubiquitin-like protein, and a candidate bioactive agent; and

b) determining the level of ubiquitin-conjugated or ubiquitin-like protein-conjugated target protein in the presence and absence of said candidate bioactive agent;

wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in Figure 2, wherein said USP-25 protein will bind to said USP-25 target protein, and wherein a difference in the level of ubiquitin-conjugated or ubiquitin-like protein-conjugated target protein in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent is capable of modulating USP-25 protein activity.

2. The method according to Claim 1 wherein said USP-25 target protein is selected from the group consisting of UBC9, SYK and calcineurin.

3. The method according to Claim 1, wherein said ubiquitin-like protein is SMT3/SUMO or NEDD8/RUBY.

4. The method according to Claim 1, wherein said USP-25 protein comprises the amino acid sequence set forth in Figure 2.

5. The method according to Claim 1, wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to a fragment of the full length amino acid sequence set forth in Figure2 wherein said USP-25 protein comprises a ubiquitin-specific peptidase domain.

6. A method for screening for a bioactive agent capable of modulating USP-25 protein activity, comprising:

a) combining a USP-25 protein, a USP-25 target protein which is conjugated to ubiquitin or ubiquitin-like protein, and a candidate bioactive agent; and

b) determining the level of ubiquitin-conjugated or ubiquitin-like protein-conjugated target protein in the presence and absence of said candidate bioactive agent;

wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in Figure 4, wherein said USP-25 protein will bind to said USP-25 target protein, and wherein a difference in the level of ubiquitin-conjugated or ubiquitin-like protein-conjugated target protein in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent is capable of modulating USP-25 protein activity.

7. The method according to Claim 6, wherein said USP-25 target protein is selected from the group consisting of UBC9, SYK and calcineurin.

8. The method according to Claim 6, wherein said ubiquitin-like protein is SMT3/SUMO or NEDD8/RUBY.

9. The method according to Claim 6, wherein said USP-25 protein comprises the amino acid sequence set forth in Figure 4.

10. The method according to Claim 6, wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to a fragment of the full length amino acid sequence set forth in Figure4 and wherein said USP-25 protein comprises a ubiquitin-specific peptidase domain.

11. A method for screening for a bioactive agent capable of modulating USP-25 protein activity, comprising:

a) combining a USP-25 protein, a USP-25 target protein which is conjugated to ubiquitin or ubiquitin-like protein, and a candidate bioactive agen;t and

b) determining the level of ubiquitin-conjugated or ubiquitin-like protein-conjugated target protein in the presence and absence of said candidate bioactive agent;

wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to the amino acid sequence encoded by the nucleic acid sequence set forth in Figure 1, wherein said USP-25 protein will bind to said USP-25 target protein, and wherein a difference in the level of ubiquitin-conjugated or ubiquitin-like protein-conjugated target protein in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent is capable of modulating USP-25 protein activity.

12. The method according to Claim 11, wherein said USP-25 target protein is selected from the group consisting of UBC9, SYK and calcineurin.

13. The method according to Claim 11, wherein said ubiquitin-like protein is SMT3/SUMO or NEDD8/RUBY.

14. The method according to Claim 11, wherein said USP-25 protein comprises the amino acid sequence encoded by the nucleic acid sequence set forth in Figure 1.

15. The method according to Claim 11, wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to an amino acid sequence encoded by a fragment of the full length nucleic acid sequence set forth in Figure1, wherein said USP-25 protein comprises a ubiquitin-specific peptidase domain.

16. A method for screening for a bioactive agent capable of modulating USP-25 protein activity, comprising:

a) combining a USP-25 protein, a USP-25 target protein which is conjugated to ubiquitin or ubiquitin like protein, and a candidate bioactive agent; and

b) determining the level of ubiquitin-conjugated or ubiquitin-like protein-conjugated target protein in the presence and absence of said candidate bioactive agent;

wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to the amino acid sequence encoded by the nucleic acid sequence set forth in Figure 3, wherein said USP-25 protein will bind to said USP-25 target protein, and wherein a difference in the level of ubiquitin-conjugated or ubiquitin-like protein-conjugated target protein in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent is capable of modulating USP-25 protein activity.

17. The method according to Claim 16, wherein said USP-25 target protein is selected from the group consisting of UBC9, SYK and calcineurin.

18. The method according to Claim 16, wherein said ubiquitin-like protein is SMT3/SUMO or NEDD8/RUBY.

19. The method according to Claim 16, wherein said USP-25 protein comprises the amino acid sequence encoded by the nucleic acid sequence set forth in Figure 1.

20. The method according to Claim 16, wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to an amino acid sequence encoded by a fragment of the full length nucleic acid sequence set forth in Figure1, wherein said USP-25 protein comprises a ubiquitin-specific peptidase domain.

21. A method for screening for a bioactive agent capable of modulating lymphocyte activation, comprising:

i) contacting a candidate bioactive agent to a lymphocyte comprising a recombinant nucleic acid encoding a USP-25 protein;

ii) inducing activation of said lymphocyte; and

iii) determining the activation of said lymphocyte in the presence and absence of said candidate bioactive agent;

wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in Figure 2, and wherein a difference in the activation of said lymphocyte in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent is capable of modulating lymphocyte activation.

22. The method according to Claim 21, wherein said USP-25 protein comprises the amino acid sequence set forth in Figure 2.

23. The method according to Claim 21, wherein said determining the activation of said lymphocyte comprises determining the activity of the immunoglobulin heavy chain gene promoter or the nuclear factor in activated T cells (NFAT) gene promoter.

24. A method for screening for a bioactive agent capable of modulating lymphocyte activation, comprising:

i) contacting a candidate bioactive agent to a lymphocyte comprising a recombinant nucleic acid encoding a USP-25 protein;

ii) inducing activation of said lymphocyte; and

iii) determining the activation of said lymphocyte in the presence and absence of said candidate bioactive agent;

wherein said USP-25 protein comprises an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in Figure 4, and wherein a difference in the activation of said lymphocyte in the presence and absence of said candidate bioactive agent indicates that said candidate bioactive agent is capable of modulating lymphocyte activation.

25. The method according to Claim 24, wherein said USP-25 protein comprises the amino acid sequence set forth in Figure 4.

26. The method according to Claim 24, wherein said determining the activation of said lymphocyte comprises determining the activity of the immunoglobulin heavy chain gene promoter or the nuclear factor in activated T cells (NFAT) gene promoter.

27. The method according to Claim 23 or 26, wherein said determining the activation of said lymphocyte further comprises determining the expression of CD69.